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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/862,571 05/23/2001 Glenn McGall 2719.2019-001 9482

21005 7590 02/24/2003

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EXAMINER

BORIN, MICHAEL L

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 02/24/2003

9

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/862,571

Applicant(s)

McGall et al

Examiner

Michael Borin

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Dec 13, 2002
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-42 is/are pending in the application.
- 4a) Of the above, claim(s) 4, 5, 8, 10, 11, and 13-42 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3, 6, 7, 9, and 12 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 8 6) ☐ Other:

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DETAILED ACTION

Status of Claims

1. Response to restriction requirement filed 05/13/99 is acknowledged. Applicant elected, without traverse, Group I, claim 3, together with linking claims 1,2,6-9,12. Claims 4,5,10,11,13-42 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected groups. Cancellation of claims 4,5,8-11,13-42 is requested.

Further, in regard to election of species, applicant elected photolabile protecting groups, and compound of Formula II. Claims reading on the elected species are 1-3,6,7,9,12. Claim 8 is withdrawn from consideration as not drawn to elected species.

Specification

2. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)).

Claim Rejections - 35 USC § 112, second paragraph.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-3,6,7,9,12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection is made for the following reasons:

A. Claim 1: It is not clear whether the objective of the method is to reduce non-specific binding of the target molecule to oligonucleotides located on "designated" or "protected" regions of the surface. Since step b) of the method allows for introducing negatively charged phosphate residue (which is supposed to reduce non-specific binding) into either one or both of these regions, it is not clear how introducing this group into one specific region (e.g., protected region) will reduce non-specific binding in another region (i.e., designated region).

B. It is not clear how use of phosphoroamidate (such as elected species of formula II) will result in formation of phosphate.

Phosphate, according to a dictionary definition is a $(\text{PO}_4)^{-3}$ ion, or a compound comprising $(\text{PO}_4)^{-3}$ (see, e.g., on-line Webster Dictionary, <http://www.m-w.com/cgi-bin/dictionary?book=Dictionary&va=phosphate>). Then, it is not clear

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how a compound of Formulas I or II, which a) have different valency, and b) do not have negatively charged groups, can introduce $(\text{PO}_4)^{-3}$ group as claimed.

C. Claim 3. The claims recites, in step 3) repeating step 2) of the claims 1-120 times. It is not clear whether step b) of claim 1 is also being repeated after each reiteration of step a).

Further, claim 3 lacks internal antecedent basis, as step 3), which addresses repetitive attachment of nucleotides to oligonucleotides, addresses it as reiteration of step 2); the latter step, however, is drawn to attachment of a nucleotide to a linker monomer, not to an oligonucleotide.

Claim Rejections - 35 USC § 112, first paragraph.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-3,6,7,9,12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for reducing non-specific binding of a particular protein (fluorescent protein conjugate phycoerythrin-streptavidin), does not reasonably

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provide enablement for reducing non-specific binding of any unspecified molecule. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

5. The claims are drawn to reducing non-specific binding of a target molecule by introducing negatively charged phosphate residue in designated or protected regions of the surface of an array. As compound that introduces the phosphate group is phosphoramidite of Formula I or II (see claim 11). A target molecule, as disclosed on p. 10 of specification is any molecule which is contained in a biological sample and is capable of binding (hybridizing) to oligonucleotides on an array. A biological sample is blood, urine, tissue, etc. As any of the molecules present in such sample is capable of binding to the surface of the array, the question is whether specification describes or provides guidance for the claimed universal effect of the negatively charged phosphate residues against non-specific binding of any of plethora of "target molecules". Aside from the issue that the elected species of formula II do not seem to render a negatively charged phosphate residue (see rejection under 35 U.S.C. 112, second paragraph, above), the only example present in specification demonstrates reduction of binding of a specific protein, namely fluorescent protein conjugate

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phycoeretrin-streptavidin (Example 1). Evidently, biological samples contain plethora of molecules differing both in their chemical activity (i.e., with different affinity to react with phosphophate group), and charge (i.e., negatively or positively charged). Thus, any positively charged molecule, e.g. a positively charged protein, would be attracted, rather than repulsed by the negative charge of the phosphate group, the effect that would increase rather than decrease non-specific binding. Specification does not provide any guidance on how to achieve reduction of binding for any "target molecule", nor it offers examples other than Example 1 (in which, in addition, the sequence of connecting of linkers, monomers, and "phosphate" compound is different from the sequence claimed in the claims currently under examination). Prior art teaches phosphoroamidites as oligonucleotide functionalizing reagents (see, e.g., US Patent 4,914,210) but do not teach that these compounds "reduce non-specific binding of a target molecule".

In view of the above, it is the Examiners position that with the insufficient guidance and working examples and in view of unpredictability and the state of art one skilled in the art could not make and/or use the invention with the claimed breadth without an undue amount of experimentation.

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6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (703) 305-4506. Dr. Borin can normally be reached between the hours of 8:30 A.M. to 5:00 P.M. EST Monday to Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Michael Woodward, can be reached on (703) 308-4028. The fax telephone number for this group is (703) 305-3014.

Any inquiry of a general nature or relating the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

February 21, 2003

mlb

MICHAEL BORIN, PH.D
PRIMARY EXAMINER

